UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,486	11/29/2000	Takehiro Yatomi	1110-0280P	1332

2292 7590 10/01/2002

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/01/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/701,486	Applicant(s) YATOMI, TAKEHIRO	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-7* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

1. Claims 1, and 3-7 are pending in this application.

Claim 4 has been withdrawn from consideration as being to a non-elected invention.

Claim 2 was cancelled by the applicant in paper number 9 (Amend. C).

Claims 1-3 and 5-7 were rejected in the prior action under 35 U.S.C. 112, first paragraph for scope of enablement. Claims 1, 6, and 7 were also rejected for lack of written description. The enablement rejection has been withdrawn in light of amendments made in Amend. C.

Claim 1, 6, and 7 are newly rejected under 102(e).

Claims 1-3 and 5-7 were rejected in the prior action as obvious under 35 U.S.C. 103(a). Claims 1, 3, and 5-7 remain rejected under 35 U.S.C. § 103(a).

Specification

2. In view of the amendment to the abstract made in paper 9, the objection to the specification is withdrawn.

Claim Rejections - 35 USC § 112

3. Claims 1-3 and 5-7 were rejected in the previous office action for scope of enablement. The claims read on methods of treating and preventing autoimmune demyelinating diseases. However, as described in the office action, the art and teachings of the specification did not support claims to methods of preventing such diseases. In light of the amendments to the claims in paper 9, limiting the claims to methods of treatment, the rejection of the claims on this ground is withdrawn.

4. Claims 1, 6, and 7 were rejected in the previous office action for containing subject matter that was not described in the specification sufficiently to show that the applicant had possession of the claimed invention when the application was filed. Although the specification described only methods of using antibodies to the Fas ligand, or Fas antagonists, the claims encompassed methods of using any apoptosis-suppressing substance. In Amend. C, the applicant amended the claims to read on Fas antagonists, rather than apoptosis suppressing substances. As the application does not fully define what is meant by a Fas antagonist, the examiner is maintaining the rejection. The examiner suggests the phrase "a substance inhibiting Fas-Fas ligand binding." The examiner would accept this term because all of the embodiments disclosed by the specification have this property; the phrase has support in the specification (p. 9, lines 11-13). This language is preferred because the applicant has not provided sufficient written description to support a claim to any Fas antagonist as there is no support for a antagonists to Fas induced apoptosis other than those that inhibit Fas-Fas ligand binding.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C.

122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1, 6, and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Us Patent Number 6,399,327, issued to Wallach et al. (Wallach). These claims describe a method of treating autoimmune demyelinating diseases, including MS by administering a Fas antagonist. A Fas antagonist is being interpreted as any molecule that can inhibit Fas-ligand induced apoptosis. Application, p. 15-16 (a Fas antagonist is any substance that suppresses apoptosis in a Fas expressing cell). Wallach teaches a protein that can bind to the intracellular domain of the Fas receptor and thereby block the Fas pathway that would otherwise lead to cell apoptosis. Col. 18, line 60- col. 19, line 10. The patent teaches that these molecules may be used to treat diseases associated with cellular apoptosis, including multiple sclerosis. Col. 24,lines 16-45. The patent therefore anticipates the stated claims.

Claim Rejections - 35 USC § 103

7. Claims 1-3 and 7 were rejected in the prior action under 35 U.S.C. 103(a) as being obvious over Keana et al., U.S. Patent Number 6,184,210. As claim 6 is inherently rendered obvious by an art rejection of claim 6, and as the rejection of claim 6 in this instance stands or falls with the rejection of claim 7, claim 6 is also part of the rejection. This patent discloses an apoptosis inhibitor useful in the treatment of multiple sclerosis. Col. 3, lines37-55. The reference also discloses the use of the substance as a preventative of Fas ligand induced apoptosis in mouse liver. Col. 23, lines 34-38. Thus, a person of ordinary skill in the art would have known to use the substance in the claimed method because of the effectiveness of the substance in preventing

mouse liver cell lysis and because the patent teaches that the substance is usable to prevent multiple sclerosis. The person of ordinary skill in the art would have reasonably expected success because of the success of the in vivo testing against mouse liver apoptosis, which is also induced by the Fas ligand.

In Amend. C, the applicant traversed this rejection on the grounds that the "only disclosure in Keana et al. of MS is in column 3, lines 42-62, which discloses a "wish list "/laundry list of more than 27 diseases," and that there is no disclosure in the reference that any compound having activity against apoptosis is effective against MS. The traversal is not found persuasive. The examiner agrees that MS is disclosed only in lists. See, columns 3, lines 42-62, and on col. 7, lines 55-62 (the later list naming only six diseases). However, the examiner does not agree that this is inadequate to show obviousness. While the patent does not state that "any" compound having activity against apoptosis is effective against MS, the patent specifically states that the compounds disclosed in the patent will be effective to treat diseases "in which apoptotic cell death is either a causative factor or a result." Col. 3, lines 42-45. Thus, the patent teaches a reason for identifying all of these diseases as treatable by the disclosed methods and compositions. Because the patent explicitly identifies this reason for choosing the members of the list, it would render obvious methods of treating any these diseases by inhibiting Fas induced apoptosis.

While a broad disclosure of various embodiments of a claim does not inherently render all those embodiments obvious, such a disclosure may do so where there is guidance that would lead to the choosing of the claimed embodiment. See e.g., *In re Baird*, 29 U.S.P.Q.2d 1550, 1551-52 (CAFC 1994). In Baird, the Federal Circuit found that a claim was not rendered obvious

when it claimed a compound that was within, but not specifically identified by a prior art reference. Id. Because the prior art gave no guidance that would have lead those in the art to choose the rejected compound, the court held that the compound was not rendered obvious. P. 1552. However, such is not the case at hand.

In the present case, the reference both specifically identifies MS and provides a reason why the method would be effective for treating it. The fact that the reason is common to the other diseases does not destroy the fact that the art suggests the claimed method. Therefore, absent either a reason to suspect that the disclosed method would not work on MS, the Keana reference renders the claims above obvious.

The combination of the relationship disclosed by the patent between the disease and the Fas induced apoptosis, with the fact that the patent is dealing with compounds that inhibit anti-Fas induced apoptosis (i.e. apoptosis induced by Fas/Fas antibody interaction), would have made it obvious to one skilled in the art to use the disclosed compositions to treat any diseases associated with Fas-induced apoptosis. Because the compounds inhibit the apoptosis activity of the Fas/Fas ligand interactions, the compositions are Fas antagonists, and thereby meet the claim limitations.

One skilled in the art would have had a reasonable expectation of success because the disease actually disclosed in the patent specification (mouse liver apoptosis) shares with MS the characteristic of being caused by Fas pathway cell apoptosis. Therefore, a treatment that targets this pathway, and is disclosed as being able to treat MS because the disease is either caused by or associated with cell apoptosis, would be expected by one the art to work against MS. For these

reasons the rejection is maintained against claim 1, 3, 6, and 7, claim 2 having been cancelled from the case in Amend. C.

8. Claims 1-3, 6, and 7 were rejected under 35 U.S.C. 103(a) as being obvious over Hughes and Crispe, J. Exp. Med, Vol. 182, 1395-1401, (1995) (Hughes); in view of Holoshitz et al, U.S. Patent Number 6,098,631; and D'Souza et al., J. Exp. Med., vol. 184, pp. 2361-70 (1996) (D'Souza). Claims 1-3 describe a method of inhibiting an autoimmune demyelinating disease using an apoptosis suppressing substance, wherein the substance is a Fas antagonist, and wherein the substance suppresses Fas-Fas ligand binding. Claims 6 and 7 further limit the methods of claims 1-3 to treatment of demyelinating diseases of the Central Nervous System (CNS), and to multiple sclerosis or acute disseminated encephalomyletis respectively. The applicant has traversed the rejection in Amend. C by arguing that Holoshitz does not teach a method of treating MS, and that the purpose of the method of Holoshitz is to induce apoptosis, and that D'Souza teaches away from the involvement of Fas-Fas ligand interactions with MS. The examiner disagrees.

Hughes teaches the use of a soluble variant of Fas to inhibit apoptosis induced by the Fas-Fas ligand interaction. Hughes, p. 1395. As a variant of the Fas receptor, those in the art would assume that the operation of the variant is to inhibit Fas ligand binding to the Fas receptor-thereby inhibiting apoptosis. Further, since the use of the variant is to inhibit the Fas-Fas ligand interaction, and the activation of apoptosis pathways, the variant is clearly a Fas antagonist. However, the reference does not teach the use of the variant to treat or inhibit autoimmune demyelinating diseases. The reference is describing a method of inhibiting the apoptosis of T cells.

D'Souza teaches that the Fas-Fas ligand pathway are involved in the loss of the myelin sheath in the CNS leading to MS. See, pp. 2367-2368. The applicant's argument that D'Souza teaches away from the involvement of the Fas- Fas ligand in MS is unfounded. The reference actually teaches that the part played by those compounds may not be that of causing apoptosis, but of causing some other dysfunction in the cells that still leads to the demyelination of the cells. P. 2367, col. 2. Thus, D'Souza teaches that even if the Fas pathway does not cause cell apoptosis, it is nonetheless involved in the development of MS, and therefore a target for treatment. The rejected claims do not require that apoptosis, rather than some other effect, be inhibited. Instead, they require only that Fas antagonists be used to treat MS, by whatever action the composition may take. Because D'Souza does not indicate that Fas in uninvolved, but merely questions the form of involvement of that the Fas pathway takes, in MS, D'Souza does not teach away from the claimed inventions, but, as the applicant states, suggests towards it.

The applicant also argues that the rejection should be withdrawn because Holoshitz teaches the treatment of rheumatoid arthritis (RA), and that by inducing apoptosis rather than inhibiting it. However, the purpose of Holoshitz was not to draw a conclusion about the similarity of treatment between RA and MS, but to use Holoshitz as part of the evidence that the Fas-Fas ligand interaction was known in the art to be a part of the pathway leading to demyelinating immune diseases. See e.g., the '631 patent, col. 5, and col. 1, lines 9-20 (describing the pathway, and linking it to the autoimmune demyelinating disease multiple sclerosis), and D'Souza, pp. 2367-68 (linking Fas receptor and ligand binding with multiple sclerosis). Thus, the disclosure of Holoshitz was intended to be seen in light of D'Souza rather

than independent from it. The fact that Holoshitz teaches a different method with respect to a different disease is not relevant to the rejection made.

What is indicated by the combination of the teachings of the three references is that the Fas pathway is involved in the development of MS, and that a method of treatment targeting the pathway would have been obvious to one of ordinary skill in the art. D'Souza and Holoshitz demonstrate both knowledge of the involvement of the Fas pathway in MS, and a knowledge of the operation of the Fas pathway itself. Due to this knowledge, although Hughes does not teach the use of the variant to prevent autoimmune demyelinating diseases, it would have been obvious to one of ordinary skill in the art, who would have been aware Holoshitz and D'Souza references, to use the Hughes variant to treat MS. This is because the method of Hughes is targeting the same ligand/receptor interaction that is responsible for causing multiple sclerosis. Cf. Hughes, p. 1395, ¶2, and D'Souza pp. 2367-68. Because multiple sclerosis is an autoimmune demyelinating disease, and because the Hughes variant is a Fas pathway inhibiting substance, the methods of the stated claims would have been obvious to one of ordinary skill in the art.

One of ordinary skill in the art would have expected success in the method because of the knowledge that the Hughes variant inhibited Fas-Fas ligand induced apoptosis. Since the method was effective in treating one form of Fas mediated immune disease, and as the same interaction was known to be involved in the development of MS, one skilled in the art would have had a reasonable expectation of success that the method of Hughes would also be effective against MS. For these reasons the rejection is maintained against claim 1, 3, 6, and 7, claim 2 having been cancelled from the case in Amend. C.

9. Claims 1-3 and 5-7 were rejected under 35 U.S.C. 103(a) in the prior action as being obvious over Nagata et al in U.S. Patent Number 6,348,334 in view of Holoshitz et al, in U.S. Patent Number 6,098,631 and Queen et al., in U.S. Patent Number 6,046,310. The examiner agrees with the applicant's traversal on the ground that Holoshitz does not teach the treatment of MS. The 103 rejection is therefore withdrawn.

The examiner agrees that Holoshitz does not teach a method for treating multiple sclerosis. And while Queen does teach such a compound, it is not believed that the compound of Queen is a Fas antagonist. This is because although the fusion protein of the patent has a reduced ability to cause apoptosis, it does prevent natural Fas pathway interactions from occurring.

10. Claims 1-3, 5, and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lynch et al. in U.S. Patent Number 5,830,469 in view of D'Souza. Claim 7 is also at issue as it the teaching of Fas inhibitors for the treatment of MS that is at issue. Therefore, claims 1, 3, and 5-7 are being rejected, claim 2 having been cancelled. Although the claim was identified by name in the prior rejection, it is included in the rejection, and has been argued on the record. The applicant traversed this rejection on the grounds that 1) although Lynch discloses the use of anti-Fas antibodies, it does disclose their use for treating MS, and 2) that D'Souza teaches away from the use of Fas-inhibitors to treat MS. Although the examiner agrees with the applicant that Lynch does not teach the use of the anti-Fas antibodies to treat MS, it does teach their use to inhibit apoptosis. Col. 4, lines 48-54. Further, the examiner disagrees with the applicant's assertion that D'Souza teaches away from the inhibition of the Fas pathway to treat MS for the reasons stated above. This rejection is therefore maintained.

11. Claims 1-3 and 5-7 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Lynch et al. in U.S. Patent Number 5,830,469, in view of Aoyagi in EP document 0 285 883. The applicant traversed this rejection on the grounds that Lynch does not teach that the treatment of MS, and that Aoyagi does not teach that MS may be treated by inhibiting Fas-Fas ligand interactions. The examiner agrees with the applicant's traversal and the rejection is hereby withdrawn. .

12. Claims 1, 3, 5, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keana as described above or over Hughes in view of Holoshitz and D'Souza as described above; and either of those sets of references further in view of Nagata. The rejected claims describe a method of treating an autoimmune demyelinating disease by administering a Fas antagonist, including embodiments wherein the Fas antagonist is an anti-Fas ligand antibody, and the disease is multiple sclerosis.

Keana teaches a method of treating diseases associated with Fas-induced apoptosis by administering inhibitors of the Fas apoptosis pathway. See, above. Together, Hughes, Holoshitz and D'Souza disclose teach that Fas antagonists are useful in inhibiting apoptosis (Hughes, p. 1395), and that multiple sclerosis may be treated by inhibiting Fas-Fas ligand interactions (D'Souza, pp. 2367-2368), and therefore that Fas antagonists may be used to treat MS. However, neither of these sets of references teaches the use of anti-Fas ligand antibodies.

Nagata et al. teaches the use anti-Fas ligand antibodies to treat diseases in which apoptosis of tissues and cells takes part. Col. 3, lines 55-59; col. 23, lines 52-57; and col.25, lines 18-26. Because Nagata teaches that the antibodies disclosed therein may be used to treat any disease in which Fas-ligand induced apoptosis of cells takes part, and the two sets of references

above disclose that MS may be treated by inhibiting the Fas apoptosis pathway, it would have been obvious to one skilled in the art to treat MS using the antibodies disclosed by Nagata. Because the same pathway is being inhibited in either case, one of ordinary skill in the art would have had both a motivation to use, and a reasonable expectation of success in the use of, the antibodies of Nagata to treat MS.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
September 12, 2002

JAMES HOUSEL 9/28/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600